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DEPARTMENT OF CELLULAR
AND COMPARATIVE BIOLOGY

April 23, 1973

Professor Joshua Lederberg
Department of Genetics
Stanford University School of Medicine
Stanford, California 94305

Dear Dr. Lederberg:

Thank you for your comments about Gunther Stent's views on the history of DNA and for the copy of your reply to Wyatt.

There are some half dozen letters, about 1945-47 which I read concerning the transformation phenomenon. I will send xeroxes to you when I return to the Lilly Library about May 1-10. The main points are these:

- (1) Muller was aware of the importance of transformation as genetic material, probably fragments, which paired and recombined with the host chromosome.
- (2) He considered the term 'transformation' unfortunate because it implied directed mutation as the mechanism involved.
- (3) He accepted the identification of transforming principle with DNA until Mirsky claimed it was actually nucleoprotein.
- (4) When Delbrück obtained recombinant-like "transformations" in bacteriophage, about 1946, Muller equated these with his own pneumococcus interpretation - the pairing and crossing over of the introduced phage genetic material resulting in progeny phage bearing new genotypic combinations.
- (5) Only in one aspect did Muller miss the boat. He thought that replication and attraction of homologous genetic material were related phenomena. He tried to use these new phenomena as a way to study gene replication through a like-to-like rather than complementary mechanism (and he relied heavily on Jehle's theories of gene "resonances" and similar oscillation attractions by likes despite Delbrück's insistence that Jehle's theories had little merit).
- (6) Muller believed the genetic fragments in transforming principle would be visible under electron microscopy and he urged Martha Baylor (then at Illinois) to look for this.

E.A. Carlson.

I spoke at length to Hotchkiss at the Stadler Symposium this month. He said Muller and Marshak did see the genetic implications correctly but neither he nor any of the collaborators in the DNA identification at Rockefeller were bold enough to commit themselves to this interpretation in the face of criticisms by Sonneborn, Undegren, Dobzhansky and others who espoused other genetic interpretations. The important point, of course, is that the work was not ignored, misunderstood, or delayed as Stent claims, but very vigorously interpreted by geneticists along different genetic lines.

Earlier Muller in 1938 to 1940 corresponded with Stadler and Delbrück about the significance of ultraviolet absorption and mutation frequency. Muller, Schultz, Stadler, Delbrück and others believed, erroneously, that the DNA served a scaffolding function which, when broken by UV, caused proteins to alter their position or shape and thereby result in mutation. I think they felt this way because Stanley's TMV analysis a few years earlier had convinced them (especially Muller) that genes were protein because TMV was nearly 95% protein. In one of his letters about this time Muller emphasizes the importance of pursuing nucleic acid research because it was so closely tied in to mutagenesis studies.

There are several references in Muller's letters about your work and the importance he attributed to it (especially the sexuality in bacteria). I will try to get copies of these for you, too.

I don't know if Robert Olby has corresponded with you. He has been working on a history of DNA and molecular biology. His knowledge of genetics is much better now than it was a few years ago when he first began interviews for this book. I saw him in January in N. Y. C. and he had just come back from Rockefeller University where he had discussed the transformation story in detail.

I hope you have copies of Muller's early papers on gene theory (Variation due to change in the individual gene; The gene as the basis of life; Physics in the attack on the fundamental problems of genetics). If not, let me know and I shall send xerox copies to you.

What you say about the paucity of source material from the participating geneticists is very true in my own experience. Some scientists feel very insecure about their reputations and they prune their correspondence of their errors and controversies. This is true of Sturtevant's papers at Cal Tech and, from discussion I've had with him, of Sonneborn's which he will donate some day. Muller was honest enough to save everything and it is possible to see how his ideas developed and what influences dominated his thinking at different times in his life. The only restrictions Mrs. Muller and I worked out were to put aside, for 25 years, letters of recommendation, grant evaluations, and personal family health matters that would embarrass the careers of living and active individuals.

Sincerely yours,



Elof Axel Carlson

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